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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/202,681	12/23/1999	ERIC J. MATHUR	09010/044001	3238

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EXAMINER
HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 10/17/2002

36

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/202,681	MATHUR ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 13-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *1,2,10 and 11* is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8, 12* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

Applicants cancellation of claim 12, amendment of claims 1-11 and addition of new claims 13-28, Paper No. 34, 7/22/2002, is acknowledged. Claims 1-11 and 13-28 are still at issue and are present for examination.

Applicants' arguments filed on 7/22/2002, Paper No. 34, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/22/2002 has been entered.

Drawings

The drawings filed on 12/23/1999 are objected to for the reasons stated on the from PTO-948 included with Paper No. 7, 6/16/2000.

Claim Objections

Claims 9, 10, 14 are objected to because of the following informalities:

Claim 9 recites "...transfecting **the** cell with the vector of claim 6" It is suggested that this be amended to recite "...transfecting **a** cell with the vector of claim 6"

Claim 10 recites "...at least 70% identical to **an** amino acid sequence as set forth in SEQ ID NO: 28." It is suggested that this be amended to "...at least 70% identical to **the** amino acid sequence as set forth in SEQ ID NO: 28." so as to be consistent with other claims and remove any potential confusion about what is being claimed.

Claim 14 recites "...SEQ ID NO:28." It is suggested that this be amended to "...SEQ ID NO:28,"

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5, 15-17, 18, 19, 20 and 21, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 is indefinite in that it is confusing in that it is drawn to an isolated polynucleotide encoding a thermostable phosphatase, or an enzymatically active fragment thereof comprising a polynucleotide having at least 70% identity to a member selected from the group consisting of: (a) a polynucleotide encoding a phosphatase or (b) a polynucleotide complementary to (a). By definition, the claimed polynucleotide

cannot have at least 70% identity to (b) the complement of a polynucleotide which encodes a phosphatase, that is the polynucleotide of (a), if in fact a limitation of the claimed polynucleotide is that it encodes a phosphatase. Since the claimed polynucleotide cannot have at least 70% identity to (b), it is suggested that his part of the claim be removed form those reference polynucleotides to which the claimed polynucleotide has identity.

Newly added claims 15-17, 20 and 21 each recite "...wherein the group further consists of a polynucleotide comprising at least 15 contiguous bases of the polynucleotide of (a) or (b)..." or something similar to this recitation. These claims are unclear in their reference to "the group" and how these dependent claims further limit the claims from which they depend. For example, claim 1 is drawn to an isolated polynucleotide which encodes an amino acid sequence of SEQ ID NO: 28 or the complement of such a polynucleotide. Claim 15 which is dependent on claim 1, further specifies that "the group further consists of a polynucleotide comprising at least 15 contiguous bases of the polynucleotide of (a) or (b) and hybridizes with specificity to a polynucleotide that encodes a polypeptide having activity as a phosphatase under specific hybridization conditions. It is unclear if applicants are attempting to broaden rather then narrow the scope of the claim from which claim 15 depends.

Claim 15 is further indefinite in the recitation of "hybridizes with specificity ...under hybridization conditions comprising 0.9M NaCl, 50 mM NaH_2PO_4, and 0.5% SDS. " as the conditions under which the hybridization reaction is performed is unclear absent a temperature at which the hybridization is performed. Nucleic acids which will

hybridize with specificity under some hybridization conditions will not necessarily hybridize with specificity under different conditions.

Claims 16, 17, 20, 21, 22-28 are each indefinite in the recitation of "hybridizes with specificity"(claims 16, 17, 20 and 21), "hybridizes under stringent conditions" (claim 22, 24-28 dependent from), "hybridizes to a polynucleotide" as these terms are unclear absent a statement of the conditions under which the hybridization reaction is performed. Nucleic acids which will hybridize under some hybridization conditions will not necessarily hybridize under different conditions.

Claims 18 and 19 are each indefinite in that they are each drawn to the phosphatases of claims 10 and 11, wherein the phosphatases comprise at least 30 contiguous amino acid residues. Claims 10 and 11 are each drawn to a phosphatase which is at least 70% identical to SEQ ID NO: 28. SEQ ID NO: 28 is a 260 amino acid phosphatase of the instant invention. It is believed that the phosphatases of claims 10 and 11 each comprise at least 30 contiguous amino acid residues, and thus claims 18 and 19 do not further limit claims 10 and 11 from which they depend.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3, 4, 6, 7, 8, 9, 13, 15-17, 20, 21 and 22-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection is stated in the previous office action.

Claims 13, 3, 4, 6, 7, 8 and 9 are drawn to an isolated polynucleotide (DNA or RNA) selected from the group consisting of: (a) a polynucleotide having at least 70 % identity to a polynucleotide that encodes the polypeptide sequence of SEQ ID NO: 28, or enzymatically active fragments thereof, wherein the polypeptide has phosphatase activity and (b) a polynucleotide complementary to (a)(claims 13, 3, 4, vectors and host cells comprising and methods using said polynucleotide (claims 6, 7, 8 and 9). Claims 15-17, 20 and 21 are drawn to polynucleotides of claims 1, 2, 5, 13, and 14, respectively, further comprising of at least 15 contiguous bases in length that will hybridize to a polynucleotide which encodes a phosphatase. Claims 15-17, 20 and 21 are included in this rejection if it is applicants intent to claim a polynucleotide outside the scope of the genus claimed by the claim from which each of these claims depend (See above 112 2nd paragraph rejection). Claims 22-28 are drawn to a polynucleotide probe comprising a nucleic acid sequence consisting of a sequence that hybridizes under stringent conditions to a polynucleotide encoding a polypeptide sequence of SEQ ID NO: 28, or a polypeptide having at least 90% identity to the sequence of SEQ ID NO: 28 or a complement thereof.

The specification, however, only provides the representative species of claimed proteins and polynucleotides represented by SEQ ID NO: 28 and the polynucleotide which encode this protein. There is no disclosure of any particular structure to function/activity relationship in the disclosed species. The specification also fails to describe additional representative species of these proteins, DNAs, host cells and methods by any identifying structural characteristics or properties other than the characteristics recited in claims, for which no predictability of function is apparent.

The genus of proteins, DNAs and host cells that are claimed is a large variable genus with potentiality of comprising or encoding many different proteins. Therefore, many functionally unrelated DNAs, proteins, host cells and methods are encompassed within the scope of these claims. The specification discloses the species encompassed by SEQ ID NO: 19 of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus which reads on not only all naturally occurring thermostable phosphatases and their encoding nucleic acids, but also on mutant thermostable phosphatases as well as enzymes of undisclosed function and their encoding nucleic acids. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised interim guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Applicants traverse this rejection as it applied to the claims prior to applicants amendment on the basis that applicants have amended the claims 13 and 14 such that each of the claimed polynucleotides encode a polypeptide having phosphatase activity. While this is acknowledged for claim 14, which has thus not been included in this rejection, this is not true for claims13, 3, 4, 6, 7, 8 and 9 which remain rejected under this statue and applicants arguments regarding these claims is moot absent this functional language. Applicants have added new claims 15-21, apparently to "separate out the issues concerning claims directed to polynucleotides comprising at least 15 contiguous bases of the claimed polynucleotides and polypeptides comprising at least 30 amino acids of the claimed polypeptides, but it remains unclear if this will be accomplished by the addition of these claims, which have been rejected under 112 2nd paragraph above.

Thus applicants argument with respect to written description must by default be made to support the removal of claims 15-17, 20, 21, 22-28 from this rejection. As discussed above claims 15-17, 20 and 21 have been included in this rejection because to the extent that applicants intent is to claim a polynucleotide comprising at least 15 contiguous bases of (a) or (b) and which hybridizes with specificity to a polynucleotide that encodes a phosphatase.

Applicants argue that one of the defined functions of the polynucleotides of the invention having at least 15 contiguous bases is that they can be used as probes for identifying polynucleotides that encode polypeptides. While those polynucleotides of the instant invention consisting of at least 15 contiguous bases of the polynucleotide which encodes SEQ ID NO: 28 would maintain this function, it remains to be seen if those polynucleotides comprising at least 15 contiguous bases of the polynucleotide

which encodes SEQ ID NO: 28, wherein only the 15 contiguous bases maintain the usefulness as a "hybridization probe" would maintain the same function.

With respect to applicants argument that a phosphatase having 30 contiguous amino acids of an amino acid sequence which is at least 70% identical to SEQ ID NO: 28, based on the revised interim guidelines concerning compliance with written description requirement of U.S.C. 112 first paragraph and example 14, applicants conclusion that since the guidelines recognize that written description is met for a genus of polypeptides that have 70% identity to SEQ ID NO: 28, the polypeptides having 30 contiguous amino acids of the genus of the polypeptides must also meet written description requirements is not persuasive. Applicants attention is directed to fact that the genus of phosphatases having 30 contiguous amino acids of an amino acid sequence which is at least 70% identical to SEQ ID NO: 28 is far larger than the genus of phosphatases that have 70% identity to SEQ ID NO: 28, and thus the analogy does not hold.

Applicant is referred to the revised interim guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 3, 4, 6, 7, 8, 9, 13, 15-17, 20, 21, 22-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for enzymatically active proteins having the amino acid sequence at least 70% identical to SEQ ID NO: 28 or enzymatically active fragments thereof, as well as polynucleotides which encode these proteins, does not reasonably provide enablement for those proteins which merely comprise 30 amino acids of SEQ ID NO: 28 or the polynucleotides which encode said proteins.

The rejection is stated in the previous office action.

Claims 3, 4, 6, 7, 8, 9, 13, 15-17, 20, 21, 22-28 are so broad as to encompass any polynucleotide having at least 70% identity to a polynucleotide that encodes SEQ ID NO: 28, vectors, and host cells comprising said polynucleotide and methods of expressing said polynucleotide (claims 13, 3, 4, 6, 7, 8, 9), any polynucleotide comprising at least 15 contiguous bases of a polynucleotide which hybridizes with specificity to a polynucleotide that encodes a phosphatase (claims 15-17, 20 and 21), any polynucleotide probe comprising any nucleic acid sequence consisting of a sequence that hybridizes to a polynucleotide encoding a polynucleiotide encoding a polypeptide of SEQ ID NO: 28 or at least 90% identical to SEQ ID NO: 28 (claims 22-28). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims. The claims rejected under this section of U.S.C. 112, first paragraph, place minimal structural and no functional limits on the claimed polynucleotides. Since the nucleic acid sequence of a polynucleotide determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the polynucleotides' structure relates to its function. However, in this case the disclosure is limited to those

polynucleotides that encode the phosphatase having the amino acid sequence of SEQ ID NO: 28.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any polynucleotide with the defined structural limitations, because the specification does not establish: (A) regions of the polynucleotide structure which may be modified without its functional activity; (B) the general tolerance of the claimed polynucleotides to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleic acid residue of the polynucleotide with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the desired function and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well

understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those polynucleotides of the claimed genus.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of nucleic acid modifications of any polynucleotide. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Applicants argue that the rejection under 35 U.S.C. §112, first paragraph is not proper because the specification teaches the complete nucleotide and amino acid sequences of the phosphatase of SEQ ID NO:28, protocols for using the DNA of SEQ ID NO:19 as a probe, and a protocols for testing for enzymatic activity, thermostability, and pH optima and methods for producing variants of a disclosed sequence are within the skill of the ordinary artisan. This is not persuasive because while methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan producing variants as claimed by applicants requires that one of ordinary skill in the art know or be provided with

guidance for the selection of which of the infinite number of variants have the claimed functional property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification.

Claim 5 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention of claim 5 appears to employ a novel DNA contained in ATCC Deposit No. 97379. Since the DNA contained in ATCC Deposit No. 97379 is essential to the claimed polynucleotide, it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The deposit is not fully disclosed, nor has it been shown to be publicly known and freely available. The enablement requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the DNA contained in ATCC Deposit No. 97379.

It is noted that applicants have deposited the organisms but there is no indication in the specification as to public availability. If the deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an

attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, applicants may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

1. during the pendency of this application , access to the invention will be afforded to the Commissioner upon request;

2. all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

3. the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and

4. the deposit will be replaced if it should ever become inviable.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application

by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 22-28 are rejected under 35 U.S.C. 102(e) as being anticipated by Hirschberg et al. (U.S. Patent No: 5,792,903).

Hirschberg et al. teach a purified and isolated DNA sequence encoding lycopene cyclase. The cDNA taught by Hirschberg et al. is a 4928 base pair sequence of DNA with an open reading frame from 2029-3261 of SEQ ID NO: 1. Hirschberg et al. teach approximately 2000 bp of sequence upstream of the lycopene cyclase open reading frame and included in this region is a region from nucleotide 1506 to 1522 (17 nucleotides) that is 100 % identical to SEQ ID NO: 19 and thus Hirschberg et al. teach an isolated polynucleotide (probe) comprising a nucleic acid sequence consisting of a sequence that hybridizes under stringent conditions to a polynucleotide (SEQ ID NO: 19) encoding a polypeptide sequence of SEQ ID NO:28. Hirschberg et al. also teach this polynucleotide probe further comprising a sequence of at least 150 bases, thus claims 22-28 are anticipated.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned

are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard Hutson, Ph.D.
Patent Examiner
Art Unit 1652
October 16, 2002